Icovamenib, an Investigational Oral Small Molecule for the Treatment of Diabetes, Activates Mechanisms that Support Metabolic Health

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Biomea Fusion, Inc.

We Aim to Cure™

Icovamenib – an Investigational Oral Small Molecule in Clinical Development for the Treatment of Diabetes

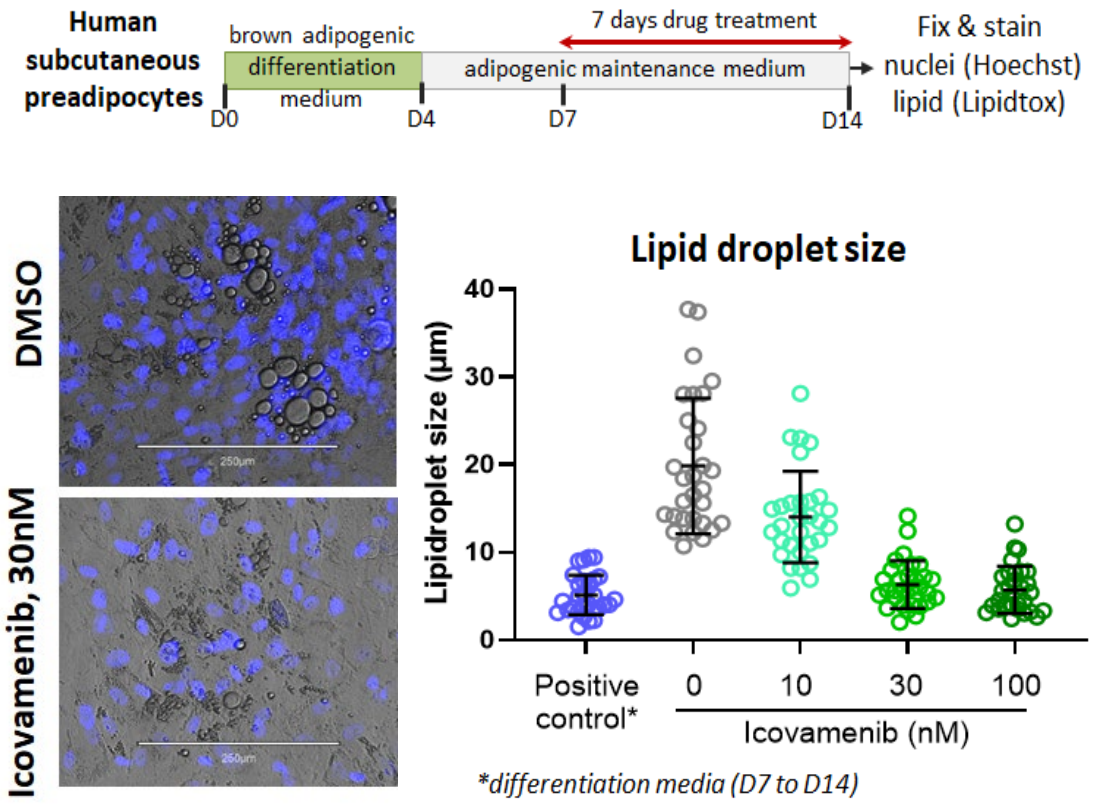
- Icovamenib MOA:
  - Glucose-dependent beta cell proliferation and enhanced insulin production and secretion, in preclinical models
  - Downmodulation of menin, a transcriptional regulator involved in beta cell proliferation and biology
- In T2D patients failing standard of care, a 12-week course of icovamenib resulted in durable HbA1c reduction and C-peptide increase through 52 weeks
- **Potential to be first-in-class beta cell restorative therapy for the treatment of type 1 and type 2 diabetes**

- **Combination treatment: Icovamenib enhanced the efficacy of low dose semaglutide in obese ZDF rat model of T2D[1]**
  - Superior body weight reduction vs low dose semaglutide
  - Weight reduction driven by fat mass loss
  - Preservation of lean mass

[1]*Somanath, et al. (ADA) Diabetes 2025;74 (Supplement_1):870-P*

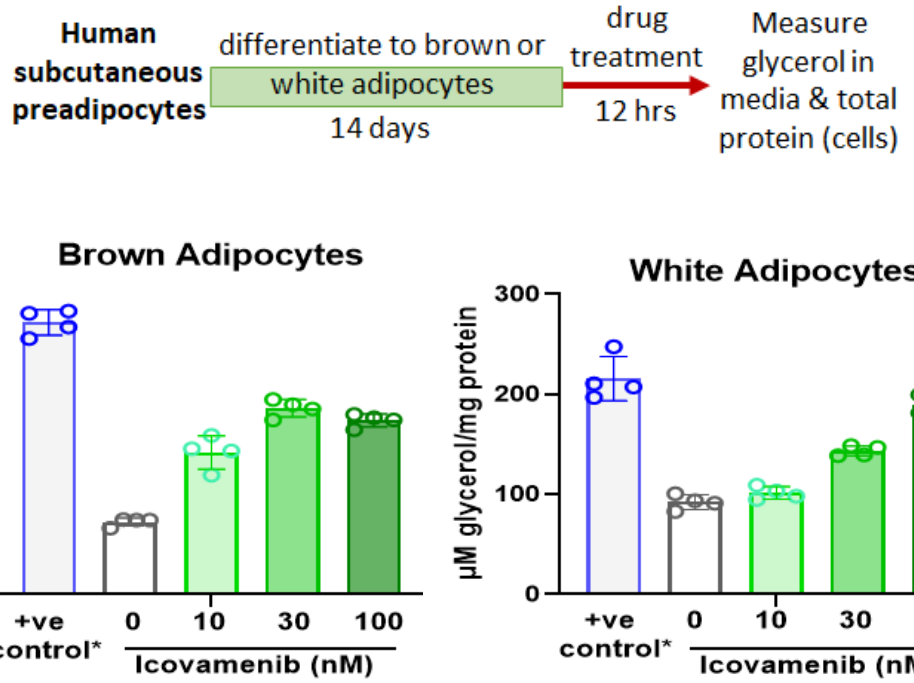
Icovamenib Promoted Lipolysis in Primary Human Adipocytes

1. Reduction in Lipid Droplet Size



*differentiation media (D7 to D14)

2. Enhanced Glycerol Release

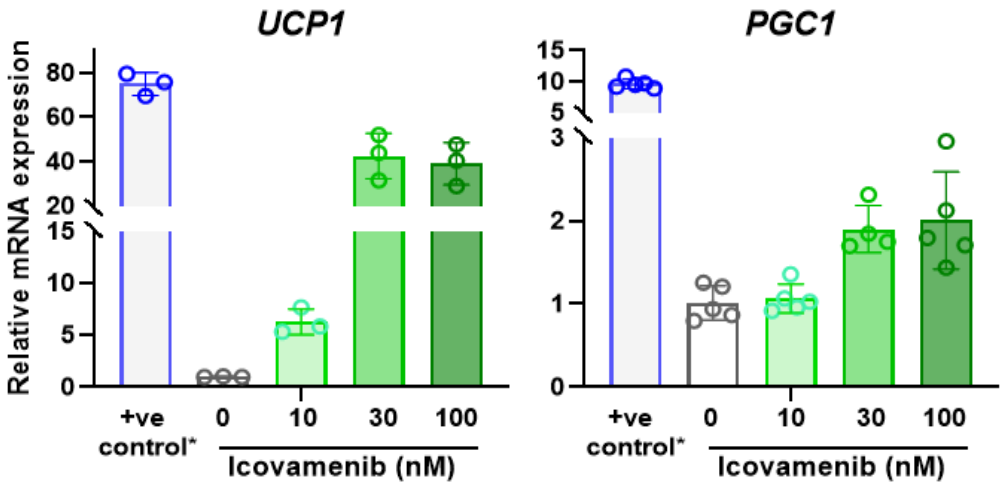


*1 mM isoproterenol

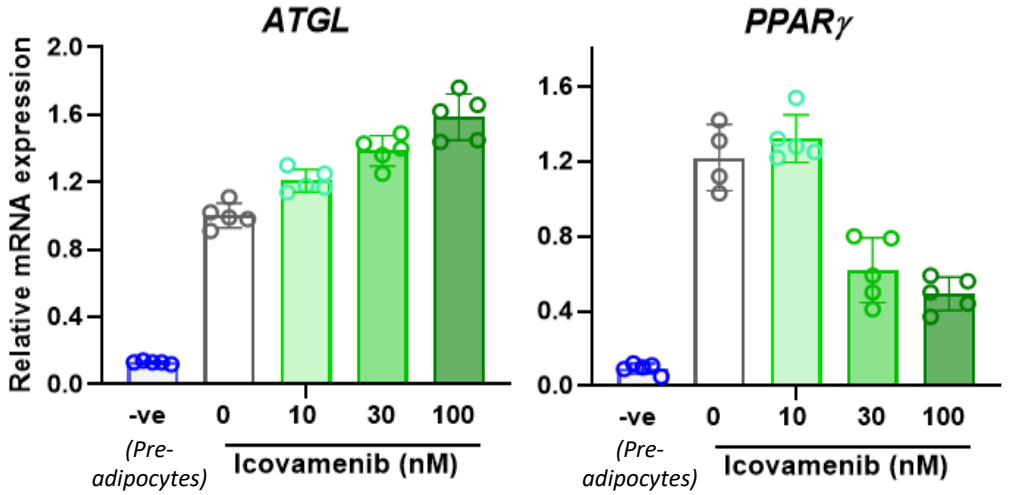
Icovamenib Promoted Effects Indicative of Lipolysis and Fat Browning in Primary Human Adipocytes

3. Upregulation of Thermogenic and Lipolytic Genes

Human Brown Adipocytes‡



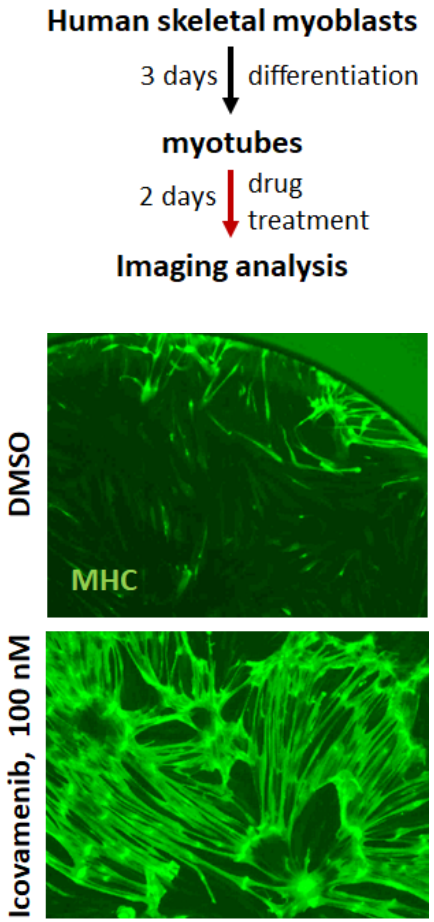
Human White Adipocytes‡

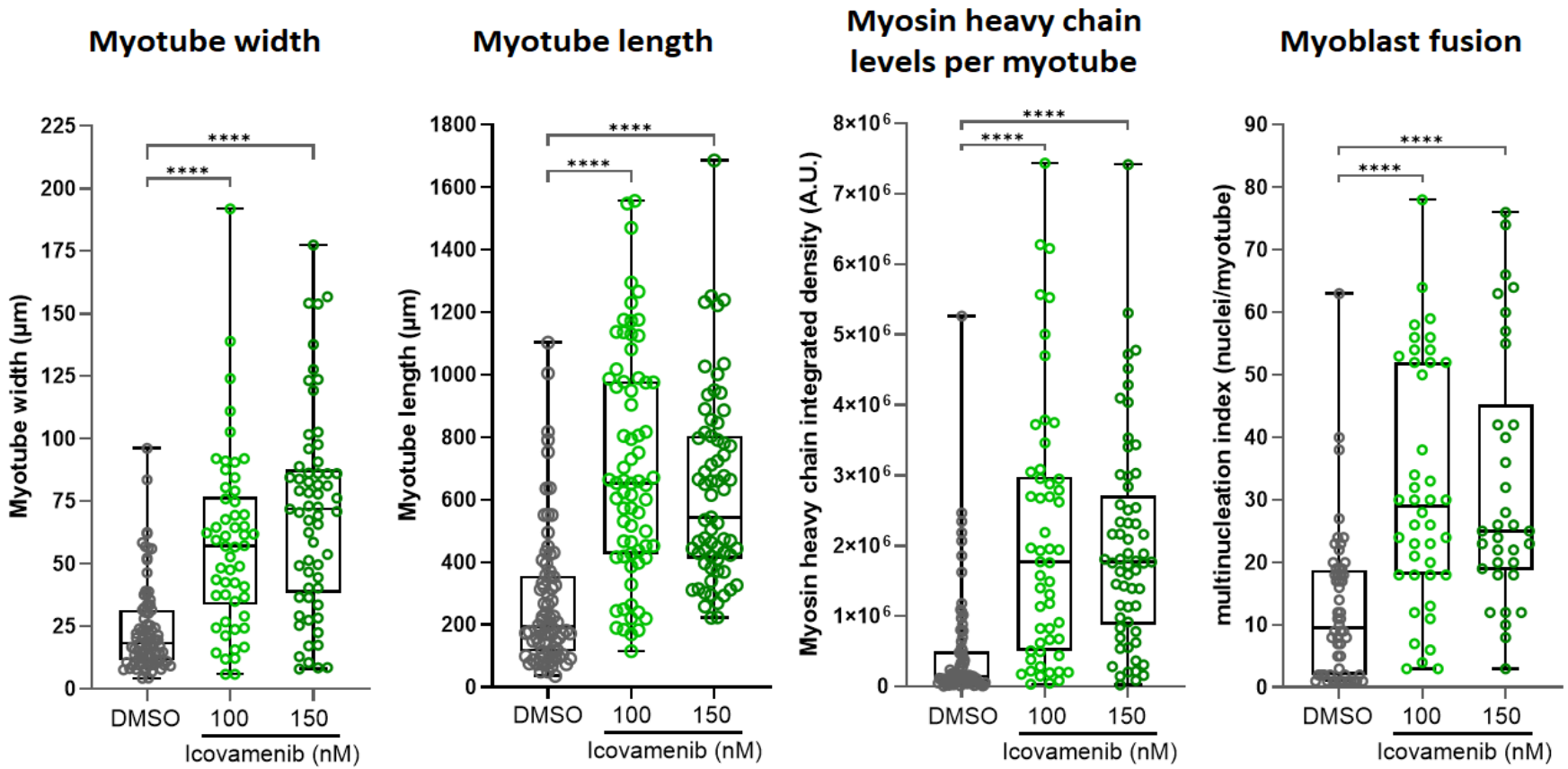


**differentiation media (D7 to D14)*

‡ Differentiated from subcutaneous preadipocytes
Cyclophilin A was used as housekeeping gene for normalization
ATGL, adipose triglyceride lipase; PGC1, peroxisome proliferator-activated receptor gamma coactivator-1; PPARγ, peroxisome proliferator-activated receptor gamma; UCP1, uncoupling protein 1

Icovamenib Induced Myogenic Effects in Human Skeletal Myoblast-derived Myotubes





Conclusions

- The collective preclinical findings provide insights into icovamenib's potential to activate mechanisms that support metabolic health, including enhanced glycemic control, fat reduction and muscle preservation.

Icovamenib-Induced Effects

- **Selective beta cell proliferation**
  - Hyperglycemia-dependent
- **Increased expression of**
  - **GLP-1** *(gut cells)*
  - **GLP-1 receptor** *(ex vivo human islets)*

→
- **Improved beta cell mass & function**
- **Improved incretin effects**

- **Activation of lipolysis & energy expenditure** *(ex vivo human adipocytes)*
- **Activation of myogenic effects** *(ex vivo human muscle cells)*

→
- **Fat loss**
- **Muscle preservation**

Anticipated Clinical Impact

- **Improved glycemic control**
  - Increase insulin secretion
  - Lower blood glucose (HbA1c)
- **Weight loss while maintaining muscle health and function**
- **Compliment & enhance efficacy of GLP-1 based therapies**

Clinical Trials in Progress

- Study #211 (NCT07502495)
- OPAL study (ISRCTN10203365)
- Study #212 (NCT07502508)